REMARKS

Applicants wish to thank the Examiner, Dr. Belyavskyi, and his supervisor, Dr. Chan, for their time and helpful discussion during a telephonic interview conducted on May 7, 2003.

Reconsideration of the present application in view of the present amendments and the following remarks is respectfully requested. Claims 20-23, 35, and 36 are currently pending. Claim 35 was withdrawn from consideration by the Examiner for being directed to a non-elected invention. Therefore, claims 20-23 and 36 are currently under examination. Applicants hereby cancel claim 35 without prejudice to further prosecution of this subject matter in a related divisional, continuation, or continuation-in-part application. Applicants have amended claims 20-23 and 36 to more clearly define the subject matter encompassed by Applicants' invention and to place the claims in condition for allowance. Support for the amended claims may be found in the specification, for example, at page 25, lines 17-24; page 35, lines 20-30 (Example 4); and SEQ ID NO:1. No new subject matter has been added.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (ENABLEMENT)

The PTO rejects claims 20-23 and 36 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The PTO concedes that the specification is "enabling for a method of detecting the presence of Fkh^{sf} encoded by amino acid sequence of SEQ ID NO:2" using an antibody that binds to such a polypeptide, but asserts that the specification is not enabling for a method of detecting the presence of any Fkh^{sf}, or any mutant thereof as presently recited in the claim. Specifically, it is alleged that the scope of the claims is not commensurate with the subject matter enabled by the disclosure.

Applicants respectfully traverse the grounds for this rejection and submit that as disclosed in the specification and recited in the present claims, the claimed invention was fully enabled at the time the Application was filed. Applicants' invention is directed in pertinent part to a method for detecting binding of an antibody that specifically reacts with an Fkh^{sf} polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2, the method comprising contacting a biological sample with an antibody, or an antibody fragment thereof, that specifically binds to an Fkh^{sf} polypeptide comprising SEQ ID NO:2, under conditions that allow

binding of the antibody or antibody fragment to the Fkh^{sf} polypeptide; and detecting binding of the antibody, or antibody fragment thereof. In another embodiment, the invention is directed in pertinent part to a method for detecting binding of an antibody that specifically reacts with a mutant Fkh^{sf} polypeptide, which is encoded by a polynucleotide comprising (i) the sequence set forth in SEQ ID NO:1 and (ii) an insertion of the complement of a TT dinucleotide into a region of SEQ ID NO:1 that comprises the complement of the sequence set forth in SEQ ID NO:11, and that results in the complement of the sequence set forth in SEQ ID NO:12, the method comprising contacting a biological sample with an antibody, or an antibody fragment thereof, as recited, under conditions that allow binding of the antibody or antibody fragment to the mutant Fkh^{sf} polypeptide, and detecting binding of the antibody, or antibody fragment thereof.

Applicants submit that the instant specification provides explicit guidance enabling a person skilled in the art to make and use the claimed methods readily and without undue experimentation. As described in the present specification, the claimed method may be practiced by using any one of a wide variety of assays to detect binding of antibodies that are specifically reactive with the Fkh^{sf} polypeptide (SEQ ID NO:2) or with the Scurfy mutant Fkh^{sf} polypeptide (*e.g.*, at page 25, lines 17-24). Such methods may be used, for example, as diagnostic tests or during procedures for purifying Fkh^{sf} polypeptide or mutant Fkh^{sf} polypeptide (*see, e.g.,* page 20, lines 21-29; page 26, lines 1-4). Antibodies that specifically bind to Fkh^{sf} polypeptide (SEQ ID NO:2) which are used in the claimed methods may be prepared according to techniques known in the art and described in the specification (*e.g.*, page 24, line 11 through page 26, line 4, and references cited therein). For example, given the teachings of the instant application, a person skilled in the art can produce the Fkh^{sf} polypeptide according to methods known in the art and described in the specification using the disclosed polynucleotide sequence (SEQ ID NO:1) that encodes the polypeptide (SEQ ID NO:2) (*see, e.g.*, pages 13, line 29 through page 21, line 9). The polypeptide and/or unique peptide fragments thereof then may be used as immunogens for generating polyclonal antisera in an animal or for generating and isolating monoclonal antibodies (*see, e.g.*, page 24, lines 19-30; page 36, line 25 through page 37, line 10 (Examples 6 and 7)). If desired by using techniques known in the art and described in the specification, the skilled artisan may purify the antibody, make antibody fragments, or attach a

detectable label to the antibody for use in the claimed methods (*e.g.*, at page 24, lines 10-30; page 25, lines 25-30; page 27, line 16 through page 28, line 28).

The instant specification also teaches a Scurfy mutant Fkh^{sf} polypeptide that may be used to generate antibodies that specifically bind to the mutant polypeptide and that are used in the claimed methods. A mutation in the *Fkh*^{sf} gene results in the Scurfy phenotype observed in affected animals (*e.g.*, at page 9, line 29 through page 10, line 6; page 32 through page 33 (Example 1)). The polynucleotide encoding the mutant Fkh^{sf} polypeptide is described in Example 4 of the instant specification (page 35). Specifically, the mutation is a two base pair insertion into the coding portion of the *Scurfy* gene (*see e.g.*, page 32, lines 20-25; page 35). The region into which the two bases are inserted is localized to a region of SEQ ID NO:1 (encoding the wildtype Fkh^{sf} polypeptide (SEQ ID NO:2)) that corresponds to the complement of SEQ ID NO:11 (*see* page 35, lines 20-30; *see also* Fig. 1A, penultimate line). The specification further describes that the insertion alters the region corresponding to SEQ ID NO:11 to yield a region corresponding to SEQ ID NO:12 (page 35, line 29) that contains an additional TT dinucleotide (shown in bold at line 29, page 35), which is complementary to insertion of an AA dinucleotide into SEQ ID NO:1. Deducing the amino acid sequence of this mutant polynucleotide is well within the abilities of a skilled artisan. Accordingly, using methods known in the art and described in the present specification, as discussed in detail above, the skilled artisan can use this polynucleotide comprising (i) the sequence set forth in SEQ ID NO:1 and (ii) an insertion of the complement of a TT dinucleotide into a region of SEQ ID NO:1, the region comprising the complement of the sequence set forth in SEQ ID NO:11, and the insertion resulting in the complement of the sequence set forth in SEQ ID NO:12, to produce the encoded mutant polypeptide. The mutant polypeptide may be used to generate antibodies that specifically bind to the mutant and that can then be used in the claimed method.

Accordingly, Applicants submit that on the basis of the disclosure in the specification and methods known in the antibody art, persons skilled in the art can make and use the aforementioned methods readily and without undue experimentation. Applicants therefore respectfully submit that the present Application satisfies the requirements of 35 U.S.C. § 112, first paragraph, and request that the rejection of these claims be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

The PTO rejects claims 20-23 and 36 under 35 U.S.C. § 112, first paragraph, asserting that the claims are directed to subject matter that is not adequately described in the specification. The PTO concedes that Applicants had possession of a method for detecting the presence of Fkh^{sf} having the amino acid sequence of SEQ ID NO:2 using an antibody that binds to such a polypeptide, but asserts that Applicants did not have possession of a method of detecting the presence of any Fkh^{sf}, or any mutant thereof, as presently recited in the claim. Specifically, the PTO alleges that Applicants have not adequately described common structural and functional properties of species within the claimed genus. In addition, the PTO asserts that the specification does not describe detecting the presence of a mutant Fkh^{sf} comprising the steps set forth in claim 36.

The PTO also rejects claim 36 under 35 U.S.C. § 112, first paragraph, alleging that the claim introduces new matter. The Action concedes that the specification and claims "as originally filed only support a method of detecting the presence of mutant Fkh^{sf} polypeptide, comprising a step of contacting a biological sample with anti-Fkh^{sf} antibody or an antibody fragment thereof." However, the PTO asserts that the specification does not provide clear support for the presently claimed limitation of using an antibody, or fragment thereof, "that specifically binds to a mutant Fkh^{sf} polypeptide encoded by a polynucleotide comprising (i) the sequence set forth in SEQ ID NO:1 and (ii) an insertion of the complement of a TT dinucleotide into a region of SEQ ID NO:1, said region comprising the complement of the sequence set forth in SEQ ID NO:12."

Applicants respectfully traverse this rejection and submit that, as disclosed in the specification and recited in the present claims, Applicants possessed the claimed invention at the time the Application was filed. One embodiment of Applicants' invention is directed in pertinent part to a method for detecting binding of an antibody that specifically reacts with an Fkh^{sf} polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2, as discussed above. Applicants submit that the instant specification describes that the presence of antibodies that react with Fkh^{sf} polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2 may be detected using a variety of assays, for example, radioimmunoassays, ELISAs, and immunoblots (*see, e.g.,* page 25, lines 17-24). The specification further describes that antibodies

which specifically bind to Fkh^{sf} polypeptide (SEQ ID NO:2) may be prepared according to techniques known in the art and described in the specification using the disclosed novel Fkh^{sf} polypeptide and/or unique peptide fragments thereof as immunogens for generating polyclonal antisera in an animal and/or for generation and isolation of monoclonal antibodies (*see, e.g.*, page 24, line 11 through page 26, line 4, and references cited therein; page 36, line 25 through page 37, line 10 (Examples 6 and 7)). Applicants therefore submit that the present specification describes that Applicants possessed the claimed method for detecting an antibody that specifically reacts with an Fkh^{sf} polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2.

Applicants submit that the instant specification also reasonably conveys to a person skilled in the art that Applicants possessed the claimed method for detecting binding of an antibody that specifically reacts with a mutant Fkh^{sf} polypeptide, which is encoded by a polynucleotide comprising (i) the sequence set forth in SEQ ID NO:1 and (ii) an insertion of the complement of a TT dinucleotide into a region of SEQ ID NO:1, that comprises the complement of the sequence set forth in SEQ ID NO:11, and that results in the complement of the sequence set forth in SEQ ID NO:12, as discussed above. Applicants further submit that the instant specification describes the mutant Fkh^{sf} polypeptide and that claim 36 does not introduce new matter.

The present specification teaches the polynucleotide sequence (SEQ ID NO:1) that encodes the wildtype Fkh^{sf} polypeptide (SEQ ID NO:2) and teaches that a mutation in the *Fkh^{sf}* gene results in the Scurfy phenotype observed in affected animals (*e.g.*, at page 9, line 29 through page 10, line 6; page 32 through page 33 (Example 1)). The polynucleotide encoding the mutant Fkh^{sf} polypeptide is described in Example 4 of the instant specification (page 35). Specifically, and as described above, the mutation is a two base pair insertion into the coding portion of the *Scurfy* gene (*see* page 32, lines 20-25; page 35). The region of the polynucleotide sequence (SEQ ID NO:1) encoding the wildtype Fkh^{sf} polypeptide in which the two bases are inserted is localized to a region of SEQ ID NO:1 that corresponds to the complement of SEQ ID NO:11 (*see* page 35, lines 20-30; *see also* Fig. 1A, penultimate line). The specification further describes that the insertion alters the region corresponding to SEQ ID NO:11 to yield a region corresponding to SEQ ID NO:12 (page 35, line 29), which contains an additional TT

dinucleotide (shown in bold at line 29, page 35), which is complementary to the insertion of an AA dinucleotide into SEQ ID NO:1. Deducing the amino acid sequence of this mutant polynucleotide is well within the abilities of a skilled artisan, and methods describing production of the mutant Fkh^{sf} polypeptide, as well as the wildtype polypeptide, are described in the instant specification (*e.g.*, page 13, line 24 through page 21, line 9). The specification further teaches that the Scurfy mutant Fkh^{sf} polypeptide may be used to generate antibodies that specifically bind to the mutant polypeptide (*e.g.*, page 26, lines 7-12). Such antibodies may be detected as provided by methods recited in the instant claims and described in the present specification (*see, e.g.*, page 2, lines 17-24).

Applicants therefore respectfully submit that the presently claimed subject matter is adequately described by the specification in compliance with the written description requirement under 35 U.S.C. § 112, first paragraph. Applicants therefore respectfully request that these rejections be withdrawn.

Applicants respectfully submit that all claims remaining in the Application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. If the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned or Stephen Rosenman, Ph.D., at (206) 622-4900.

Respectfully submitted,

Mary E. Brunkow et al.

Seed Intellectual Property Law Group PLLC

Mae Joanne Rosok

Mae Joanne Rosok
Registration No. 48,903

MJR:sd

Enclosure:

Postcard

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

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